UNITED STATES DISTRICT COURT

DISTRICT OF NEVADA

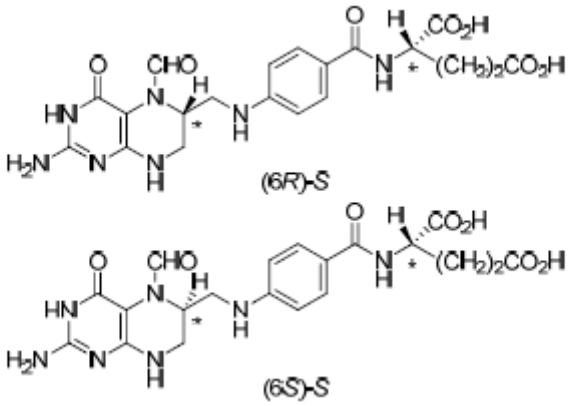
SPECTRUM PHARMACEUTICALS, INC. and UNIVERSITY OF STRATHCLYDE, Plaintiffs, vs. SANDOZ INC., Defendant.	Case No.: 2:12-cv-00111-GMN-NJK **ORDER**

Pending before the Court is the Motion for Summary Judgment (ECF No. 230) filed by Defendant Sandoz Inc. ("Defendant"). Also before the Court is the Motion for Summary Judgment (ECF No. 236) filed by Plaintiffs Spectrum Pharmaceuticals, Inc. and University of Strathclyde (collectively, "Plaintiffs"). Both motions are fully briefed. For the reasons discussed below, Defendant's Motion for Summary Judgment is **GRANTED**, and Plaintiffs' Motion for Summary Judgment is **GRANTED in part and DENIED in part**.

I. BACKGROUND

5-formyl-(6R,S)-tetrahydrofolic acid is the chemical name for a compound more commonly known as leucovorin. This compound has been used since the 1950s to prevent the toxic side-effects of methotrexate, a commonly used chemotherapy agent. U.S. Patent No. 6,500,829 col.1 ll.22–24 (filed Apr. 18, 1995). Essentially, leucovorin protects the patient's healthy cells while still allowing the methotrexate to kill the cancerous cells. *Id.* at col.1 ll.24–29. Without leucovorin, methotrexate would also kill many of the patient's healthy cells. *Id.* This use of leucovorin is known as "methotrexate rescue." *Id.* at col.1 ll.24–29.

As the name suggests, 5-formyl-(6R,S)-tetrahydrofolic acid contains an asymmetric (or chiral) center at the 6 carbon. *Id.* at col.1 ll.34–35.



This chiral center causes leucovorin to exist as a 50-50 mixture of two diastereoisomers denoted as the "6R" isomer and the "6S" isomer. *Id.* However, only the 6S isomer, known as "levoleucovorin," is the effective methotrexate rescue agent. *Id.* at col.1 ll.57–61. For this reason, scientists began attempting to separate the 6S isomer from the 6R isomer to enable administration of a higher dosage of the effective 6S isomer. Although other scientists have previously discovered methods of synthesis or isolation, these methods either produced low yields or failed to achieve reasonable purity. *See id.* at col.2 ll.13–23.

In response to the shortcomings of the prior art methods of separating and purifying levoleucovorin, a team of researchers from Plaintiff University of Strathclyde filed a patent application, which eventually issued as the '829 Patent. Specifically, the '829 Patent discloses "substantially pure" levoleucovorin compositions, which have "most preferably greater than 95%" of the (6S) isomer. *Id.* at col.4 ll.26–29. The '829 Patent describes that substantially pure 6R and 6S samples can be achieved in good yield by introducing a "chiral auxiliary group into tetrahydrofolate or a tetrahydrofolate derivative" close to the chiral center the 6 carbon. *Id.* col.2, ll.24-29. The '829 Patent further discloses that "[t]he pair of new diastereoisomers so created [could] be separated by standard techniques such as crystallisation, chromatography, solvent extraction and similar methods." *Id.* col.3 ll.42–45. The chosen method of purification

can be repeated to improve purity. *Id.* col.3 ll.54–56. "Conveniently the step may be repeated until the recovered new diastereoisomer has a purity greater than 90%." *Id.* col.3 ll.56–58.

After filing a New Drug Application ("NDA") with the FDA, Plaintiff Spectrum Pharmaceuticals, Inc. received approval to market this substantially pure form of levoleucovorin under the trade name "Fusilev®." The FDA approved Fusilev® "to treat patients diagnosed with advanced metastic colorectal cancer . . . to effect 'methotrexate rescue.'" (Pls.' Claim Construction Br. 4:2–4, ECF No. 49).

In 2011, Defendant Sandoz filed an Abbreviated New Drug Application ("ANDA") with the FDA, pursuant to 21 U.S.C. § 355(j), seeking to market a proposed generic version of Fusilev®. Defendant proposed products consisting of Levoleucovorin Calcium Injection in quantities of 175 mg/17.5 mL and 250 mg/25 mL. (Ex. 3 to Decl. of John R. Lanham at 2, ECF No. 233–3). As required by section 355(j)(2)(A)(vii), Defendant certified in its ANDA that the manufacture, use, or sale of its generic version of Fusilev® would not infringe any valid, enforceable claim of any patent that covers Fusilev®. In addition, as required by section 355(j)(2)(B)(iii), Defendant provided notice of its ANDA to the owner of the '829 Patent, Plaintiff University of Strathclyde, 21 U.S.C. § 355(j)(2)(B)(iii)(I), and to the holder of the approved NDA that is covered by the '829 Patent, Plaintiff Spectrum Pharmaceuticals, 21 U.S.C. § 355(j)(2)(B)(iii)(II). In response, Plaintiffs filed the instant action alleging infringement of the '829 Patent. (Compl. ¶¶ 21–28, ECF No. 1.)

On December 31, 2013, this Court issued a Claim Construction Order (ECF No. 199). The Court construed the primary nine (9) disputed claim terms in the '829 Patent as follows:

"mixture"	Plain and ordinary meaning
the "percentage" claim terms	Plain and ordinary meaning
"the balance of said composition consisting of the (6R) diastereoisomer"	the remaining amount of the mixture of (6S) and (6R) diastereoisomers is the (6R) diastereoisomers, and any impurities normally associated with the mixture of (6S) and (6R) diastereoisomers
"pharmaceutical composition for	a pharmaceutical composition suitable for treating

therapeutic use"	medical conditions
"pharmaceutical composition for preparing medicaments for therapeutic use for the treatment of human beings"	a pharmaceutical composition from which can be prepared a medicine suitable for treating medical conditions in human beings
"consists essentially of"	"the specified materials and those that do not materially affect the basic and novel characteristic(s) of the composition"
the "multiple dose" or "4,000 mg (4 grams)" claim terms	Plain and ordinary meaning; the pharmaceutical composition must contain enough of the (6S)/(6R) mixture to provide two or more doses of, at minimum, 2000 mg per dose of the mixture

Following claim construction, both parties filed the instant motions for partial summary judgment. Defendant asserts it is entitled to summary judgment of non-infringement of Claims 5–9 of the '829 Patent. (*See* Def.'s Mot. for Summ. J., ECF No. 229). Plaintiffs assert they are entitled to summary judgment of no invalidity in light of Rees 1986[1] and no inequitable conduct. (*See* Pls.' Mot. for Summ. J., ECF No. 236).

II. LEGAL STANDARD

The Federal Rules of Civil Procedure provide for summary adjudication when the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). Material facts are those that may affect the outcome of the case. *See Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986). A dispute as to a material fact is genuine if there is sufficient evidence for a reasonable jury to return a verdict for the nonmoving party. *See id.* "Summary judgment is inappropriate if reasonable jurors, drawing all inferences in favor of the nonmoving party, could return a verdict in the nonmoving party's favor." *Diaz v. Eagle Produce Ltd. P'ship*, 521 F.3d 1201, 1207 (9th Cir. 2008) (citing *United States v. Shumway*, 199 F.3d 1093, 1103–04 (9th Cir. 1999)). A

[1] Rees 1986 refers to the following article, Lilias Rees et al., *Asymmetric Reduction of Dihydrofolate Using Dihydrofolate Reductase and Chiral Boron-Containing Compounds*, 42 Tetrahedron 117 (1986).

principal purpose of summary judgment is "to isolate and dispose of factually unsupported claims." *Celotex Corp. v. Catrett*, 477 U.S. 317, 323–24 (1986).

In determining summary judgment, a court applies a burden-shifting analysis. "When the party moving for summary judgment would bear the burden of proof at trial, it must come forward with evidence which would entitle it to a directed verdict if the evidence went uncontroverted at trial. In such a case, the moving party has the initial burden of establishing the absence of a genuine issue of fact on each issue material to its case." *C.A.R. Transp. Brokerage Co. v. Darden Rests., Inc.*, 213 F.3d 474, 480 (9th Cir. 2000) (citations omitted). In contrast, when the nonmoving party bears the burden of proving the claim or defense, the moving party can meet its burden in two ways: (1) by presenting evidence to negate an essential element of the nonmoving party's case; or (2) by demonstrating that the nonmoving party failed to make a showing sufficient to establish an element essential to that party's case on which that party will bear the burden of proof at trial. *See Celotex Corp.*, 477 U.S. at 323–24. If the moving party fails to meet its initial burden, summary judgment must be denied and the court need not consider the nonmoving party's evidence. *See Adickes v. S.H. Kress & Co.*, 398 U.S. 144, 159–60 (1970).

If the moving party satisfies its initial burden, the burden then shifts to the opposing party to establish that a genuine issue of material fact exists. *See Matsushita Elec. Indus. Co. v. Zenith Radio Corp.*, 475 U.S. 574, 586 (1986). To establish the existence of a factual dispute, the opposing party need not establish a material issue of fact conclusively in its favor. It is sufficient that "the claimed factual dispute be shown to require a jury or judge to resolve the parties' differing versions of the truth at trial." *T.W. Elec. Serv., Inc. v. Pac. Elec. Contractors Ass'n*, 809 F.2d 626, 631 (9th Cir. 1987). In other words, the nonmoving party cannot avoid summary judgment by relying solely on conclusory allegations that are unsupported by factual data. *See Taylor v. List*, 880 F.2d 1040, 1045 (9th Cir. 1989). Instead, the opposition must go

beyond the assertions and allegations of the pleadings and set forth specific facts by producing competent evidence that shows a genuine issue for trial. *See Celotex Corp.*, 477 U.S. at 324.

At summary judgment, a court's function is not to weigh the evidence and determine the truth but to determine whether there is a genuine issue for trial. *See Anderson*, 477 U.S. at 249. The evidence of the nonmovant is "to be believed, and all justifiable inferences are to be drawn in his favor." *Id*. at 255. But if the evidence of the nonmoving party is merely colorable or is not significantly probative, summary judgment may be granted. *See id.* at 249–50.

III. DISCUSSION

A. Defendant's Motion for Summary Judgment

Defendant asserts it is entitled to summary judgment of non-infringement of Claims 5–9 of the '829 Patent. Determining infringement requires a two-step analysis: (1) "the claim must be properly construed to determine its scope and meaning;" and (2) "the claim as properly construed must be compared to the accused device or process." *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1565 (Fed. Cir. 1997). "To establish infringement of a patent, every limitation set forth in a claim must be found in an accused product or process exactly or by a substantial equivalent." *Becton Dickinson & Co. v. C.R. Bard, Inc.*, 922 F.2d 792, 796 (Fed. Cir. 1990) (citing *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1259 (Fed. Cir. 1989)). Therefore, Defendant can carry its initial burden "by pointing out that the patentee failed to put forth evidence to support a finding that a limitation of the asserted claim was met by the structure in the accused devices." *Johnston v. IVAC Corp.*, 885 F.2d 1574, 1578 (Fed. Cir. 1989). If Defendant satisfies this burden, the burden shifts to Plaintiffs, the nonmovant, to establish the existence of a genuine issue of material fact by "produc[ing] specific evidence . . . to show that the dispute exists." *See Bhan v. NME Hospitals*, 929 F.2d 1404, 1409 (9th Cir. 1991).

/ / /

1. Literal Infringement

"To establish literal infringement, every limitation set forth in a claim must be found in an accused product, exactly." *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1575 (Fed. Cir. 1995) (citing *Becton Dickinson*, 922 F.2d at 796). "Under [35 U.S.C.] § 271(e)(2)(A), a court must determine whether, if the drug were approved based upon the ANDA, the manufacture, use, or sale of that drug would infringe the patent in the conventional sense." *Glaxo*, 110 F.3d at 1569. Therefore, if a single claim limitation is not present in a proposed ANDA product, that product cannot literally infringe the claim. *See Glaxo Wellcome, Inc. v. Impax Labs., Inc.*, 356 F.3d 1348, 1351 (Fed. Cir. 2004).

Here, Defendant asserts that it cannot literally infringe Claims 5-9 under the Court's Claim Construction Order because its proposed "ANDA product will not be made, used, offered for sale, or sold within the United States, or imported into the United States as a composition for providing two or more doses of the claimed mixture of (6S) and (6R) diastereoisomers in an amount of at minimum 2,000 mg per dose." (Def.'s Mot. for Summ. J. 12:15–13:6). Specifically, Defendant asserts that, because its proposed ANDA products contain either 175 mg/17.5 mL or 250 mg/25 mL of levoleucovorin calcium injection, its proposed ANDA products do not provide enough of the (6S) and (6R) diastereoisomers to provide an amount of 2000 mg per dose. (*Id.* 13:7–24).

On the other hand, Plaintiffs argue that Defendant "will infringe Claim 5 with each act of importation into the United States of a sufficient number of its vials which together 'contain[] enough of the (6S)/(6R) mixture to provide two or more doses of, at minimum, 2000 mg per dose of the mixture.'" (Pls.' Resp. n.5, 8:24–26).

The claim limitations at issue are "said composition being of a quantity at least sufficient to provide multiple doses of said mixture of (6S) and (6R) diastereoisomers in an amount of 2000 mg per dose." *See* U.S. Patent No. 6,500,829 col.9 ll.55, 63–64. This Court construed

these limitations as follows:

> Thus, after looking first to the words of the claim and then the remaining parts of the intrinsic record, the Court finds that a person of ordinary skill in the art of organic chemistry would understand the phrase "said composition being of a quantity at least sufficient to provide multiple doses of said mixture of (6S) and (6R) diastereoisomers in an amount of 2000 mg per dose," as used in the'829 Patent, to have its plain and ordinary meaning. The words of the claims and the remaining parts of the specification do not support the construction asserted by either party. Rather, "said composition being of a quantity at least sufficient to provide multiple doses of said mixture of (6S) and (6R) diastereoisomers in an amount of 2000 mg per dose" simply requires that the pharmaceutical composition contains enough of the (6S)/(6R) mixture to provide two or more doses of, at minimum, 2000 mg per dose of the mixture.

(Ct.'s Claim Construction Order 31:20–32:4). Comparing Defendant's proposed ANDA products to Claim 5 as construed by the Court, the Court finds that Defendant's proposed ANDA products do not literally infringe Claims 5–9 of the '829 Patent because neither product contains enough of the (6S)/(6R) mixture to provide two or more doses of, at minimum, 2000 mg per dose of the mixture. Accordingly, Plaintiffs never asserted that Defendant's individual vials infringed Claims 5–9 of the '829 Patent. (Pls.' Resp. n.2, 7:27).

Although Plaintiffs attempt to establish literal infringement by asserting that an aggregation of Defendant's proposed ANDA products literally infringe Claim 5, Plaintiffs do not cite any case law to support this theory. Additionally, the Court could not find case law supporting Plaintiffs' aggregation theory. Therefore, the Court finds that a genuine issue of material fact does not exist regarding literal infringement of Claims 5–9 of the '829 Patent, and accordingly, Defendant is entitled to summary judgment of no literal infringement of Claims 5–9.

/ / /

2. Doctrine of Equivalents

"Under the doctrine of the equivalents, 'a product or process that does not literally infringe ... the express terms of a patent claim may nonetheless be found to infringe if there is 'equivalence' between the elements of the accused product or process and the claimed elements of the patented invention.'" *Duramed Pharm., Inc. v. Paddock Labs., Inc.*, 644 F.3d 1376, 1380 (Fed. Cir. 2011) (quoting *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 21 (1997)). The Supreme Court has recognized at least two legal limitations on applying the doctrine of equivalents: (1) the "all-elements rule," which bars a patentee from asserting a theory of equivalence that would entirely vitiate a particular claim element; and (2) prosecution history estoppel, which bars a patentee from asserting a scope of equivalency surrendered during prosecution. *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1323 (Fed. Cir. 2009) (citing *Warner–Jenkinson*, 520 U.S. at 39 n. 8). Moreover, when a patentee discloses but does not claim subject matter, the unclaimed subject matter is disclosed to the public. *Johnson & Johnson Assocs. Inc. v. R.E. Serv. Co., Inc.*, 285 F.3d 1046, 1054 (Fed. Cir. 2002). These limitations are questions of law to be determined by the Court. *Id.*

The "all-elements rule" provides that "[a] court may not apply the doctrine of equivalents where so doing would effectively eliminate a claim element in its entirety." *Wavetronix LLC v. EIS Elec. Integrated Sys.*, 573 F.3d 1343, 1360 (Fed. Cir. 2009) (citing *Warner–Jenkinson*, 520 U.S. at 29). However, the Federal Circuit has warned that an overly broad application of the all-elements rule may improperly "swallow the doctrine of equivalents" entirely and limit infringement to a "repeated analysis of literal infringement." *Ethicon Endo–Surgery, Inc. v. U.S. Surgical Corp.*, 149 F.3d 1309, 1317 (Fed. Cir. 1998).

Defendant asserts that the "all-elements rule" applies because application of the doctrine of equivalents would "vitiate claim 5's limitation of 'multiple doses of said mixture … in an amount of 2000 mg per dose' by disregarding the weight claimed as well as completely

ignoring the 'per dose' requirement." (Def.'s Mot. for Summ. J. 19:26–20:1). The Court finds this argument unavailing. First, the "per dose" requirement would not be ignored. Defendant concedes that its proposed ANDA product will provide doses. (Def.'s Mot. for Summ. J. 6:12–14 ("Sandoz's ANDA product will be imported and sold in ready-to-use, single-use vials of only 175 mg or 250 mg, indicated for doses of 7.5 to 75 mg per dose.")). Second, a difference in weight value does not foreclose the application of the doctrine of equivalents. *See Adams Respiratory Therapeutics, Inc. v. Perrigo Co.*, 616 F.3d 1283, 1292 (Fed. Cir. 2010) ("The recitation of a specific numerical value does not by itself foreclose the application of the doctrine of equivalents . . . [and] [t]he addition of 'at least' . . . does not change this analysis."). Rather, the "proper inquiry is whether the accused value is insubstantially different from the claimed value." *Id.* Therefore, the "all-elements rule" does not preclude the application of the doctrine of equivalents.

Additionally, the doctrine of equivalents can be limited by the public disclosure rule. Specifically, "when a patent drafter discloses but declines to claim subject matter . . . this action dedicates that unclaimed subject matter to the public." *Johnson & Johnson*, 285 F.3d at 1054. Therefore, "[a]pplication of the doctrine of equivalents to recapture subject matter deliberately left unclaimed would 'conflict with the primacy of the claims in defining the scope of the patentee's exclusive right.'" *Id.* (quoting *Sage Prods. Inc. v. Devon Indus., Inc.*, 126 F.3d 1420, 1424 (Fed. Cir. 1997)).

Defendant argues that the public disclosure rule precludes the application of the doctrine of equivalents because specification of the '829 Patent "reveals that the applicants knew of dosages in amounts similar to Sandoz's ANDA product, but chose not to claim them." (Def.'s Mot. for Summ. J. 20:4–5). However, this argument is misplaced. As the Court clarified in its Claim Construction Order, Claim 5 simply requires "that the pharmaceutical composition *contains enough* of the (6S)/(6R) mixture *to provide* two or more doses of, at minimum, 2000

mg per dose of the mixture." (32:3–4, ECF No. 199) (emphasis added). Claim 5 recites a product, not a use. The pertinent potion of the specification discloses "[w]hen used as a methotrexate rescue agent dosage of the 6S diastereoisomer of leucovorin will depend inter alia on the amount of methotrexate administered; however a typical daily dose is generally up to 150 mg. e.g. in the range from 25 to 150 mg, which is conveniently administered in divided dose." U.S. Patent No. 6,500,829 col.5 ll.15–21. This portion of the specification discloses a use. Therefore, the fact that the applicants knew of and disclosed a use of the pharmaceutical composition to administer dosages in amounts similar to Defendant's ANDA product is irrelevant to the product recited in Claim 5 and does not preclude the application of the doctrine of equivalents.

Prosecution history estoppel bars the application of the doctrine of equivalents to recapture subject matter that was surrendered during prosecution. *Hilgraeve Corp. v. McAfee Assocs., Inc.*, 224 F.3d 1349, 1355 (Fed. Cir. 2000). "There are two distinct theories that fall under the penumbra of prosecution history estoppel—amendment-based estoppel and argument-based estoppel." *Deering Precision Instruments, L.L.C. v. Vector Distrib. Sys., Inc.*, 347 F.3d 1314, 1324–25 (Fed. Cir. 2003) (citing *Elkay Mfg. Co. v. Ebco Mfg. Co.*, 192 F.3d 973, 979 (Fed. Cir. 1999)).

As to argument-based estoppel, "the prosecution history must evince a clear and unmistakable surrender of subject matter." *Conoco, Inc. v. Energy & Envtl. Int'l, L.C.*, 460 F.3d 1349, 1363 (Fed. Cir. 2006) (citing *Deering Precision*, 347 F.3d at 1326). *See also Read Corp. v. Portec, Inc.*, 970 F.2d 861, 824 (Fed. Cir. 1992) ("Every statement made by a patentee during prosecution to distinguish a prior art reference does not create a separate estoppel. Arguments must be viewed in context."). "The relevant inquiry is whether a competitor would reasonably believe that the applicant had surrendered the relevant subject matter." *Conoco, Inc.*, 460 F.3d at 1363 (quoting *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1457

(Fed.Cir.1998) (en banc)).

Plaintiffs assert that argument-based estoppel should not apply because "[t]he only statement made by the applicants was too vague to constitute 'clear and unmistakable surrender of subject matter.'" (Pls.' Resp. 25:5–6). The pertinent statement made by the applicants provides as follows:

> Claims 27, 29-31 filed herewith correspond to claims pending in the parent application of this case. New claims 32-41 were discussed during the interview in the parent case of this application. **These claims include specific limitations as to quantities of materials; forms of the materials and the process employed to prepare the materials.**

(*Id.* 25:9–11 (quoting Ex. 13 to Decl. of Amanda K. Antons at 5, ECF No. 253–13).[2] Additionally, Plaintiffs assert "[n]owhere in the voluminous file history did the applicants argue the quantity limitation as a basis to overcome a rejection premised on Rees 1986." (*Id.* 25:12–13). However, review of the file history provides otherwise.

In an Office Action dated March 7, 1996, the examiner of the '829 Patent application rejected Claims 27, 29, and 32–41 under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Rees 1986. (Ex. 13 to Decl. of John R. Lanham at 25, ECF No. 233–13). In an Appeal Brief dated March 10, 1997, applicants argued that "Claims 32–41 include more stringent quantity limitations than Claims 27 and 29 and are thus further patentably distinguish[ed] over Rees [1986]." (*Id.* at 53). Applicants further argued "[o]n the other hand, the Rees et al. article produced (6S) leucovorin in a quantity of <u>less than one gram</u>," and "[q]uantity limitations have previously been recognized as forming a portion of a pharmaceutical 'invention as a whole'." (*Id.* at 54). Applicants went on to assert that "[t]he quantity limitations set forth in the claims of this application define an aspect of the invention that is of great practical significance." (*Id.* at 55). Applicants concluded, stating "Rees et al. do

[2] Claim 27 eventually issued as Claim 1 of the '829 Patent. Likewise, Claims 32–41 issued as Claims 5–14.

not teach, suggest, or otherwise render obvious the claimed compositions in the quantity specified by Claims 27 and 29, or by Claims 32–41." (*Id.* at 56).

The Court finds these arguments made before the examiner to demonstrate patentability over Rees 1986 evince a clear and unmistakable surrender of subject matter covering pharmaceutical composition quantities less than what is required to provide two or more doses of, at minimum, 2000 mg per dose of the mixture. This clear and unmistakable surrender of subject matter precludes infringement of Claims 5–9 under the doctrine of equivalents. Therefore, because the Court finds that a genuine issue of material fact does not exist regarding literal or equivalent infringement of Claims 5–9, the Court grants summary judgment of non-infringement of Claims 5–9.

B. Plaintiffs' Motion for Summary Judgment of No Invalidity

Plaintiffs assert it is entitled to summary judgment of no invalidity in light of Rees 1986. Under 35 U.S.C. § 282, a patent is presumed valid. Because issued patents enjoy a presumption of validity, the party seeking to establish invalidity bears the burden of proving invalidity by clear and convincing evidence. *Microsoft Corp. v. i4i Ltd. P'ship*, 131 S.Ct. 2238, 2244–52 (2011). "A single prior art reference that discloses, either expressly or inherently, each limitation of a claim invalidates that claim by anticipation." *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1375 (Fed. Cir. 2005) (citing *Minn. Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1565 (Fed. Cir. 1992)). Additionally, "[a]nticipation requires clear and convincing proof that a single prior art reference 'not only disclose[s] all of the elements of the claim within the four corners of the document, but ... also disclose[s] those elements arranged as in the claim.'" *Cheese Sys., Inc. v. Tetra Pak Cheese & Powder Sys., Inc.*, 725 F.3d 1341, 1351 (Fed. Cir. 2013) (quoting *Net MoneyIN, Inc. v. VeriSign, Inc.*, 545 F.3d 1359, 1369 (Fed. Cir. 2008)). Whether a patent claim is invalid as anticipated is a question of fact. *IPXL Holdings, L.L.C. v. Amazon.com, Inc.*, 430 F.3d 1377,

1380 (Fed. Cir. 2005).

Plaintiffs assert that Rees 1986 did not anticipate the '829 Patent claims because "a pharmaceutical composition" and "a mixture of (6S) and (6R) diastereoisomers," which are elements recited in each independent claim of the '829 Patent, were not disclosed in Rees 1986. (Pls.' Mot. for Summ. J. 17:3–6).

1. Rees 1986

One dispute among the parties involves the interpretation of two figures within Rees 1986. The first figure, Figure 1b, provides the "Hplc analysis of Tetrahydrofolate derivative diastereoisomers:"

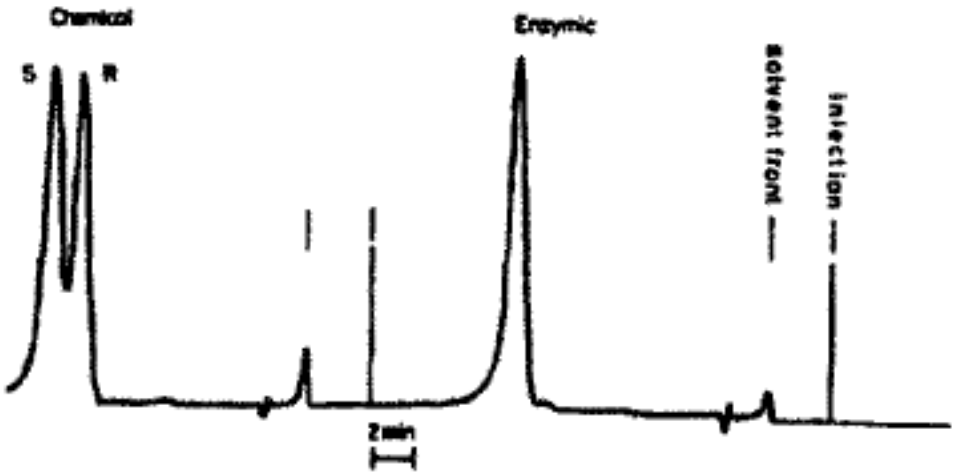


Figure 1b Hplc analysis of Tetrahydrofolate derivative diastereoisomers

(Ex. 4 to Decl. of Amanda K. Antons at 4, ECF No. 237–4). The second figure, Figure 2, provides the "250 MHz nmr of derivatised Tetrahydrofolate diastereoisomers:"

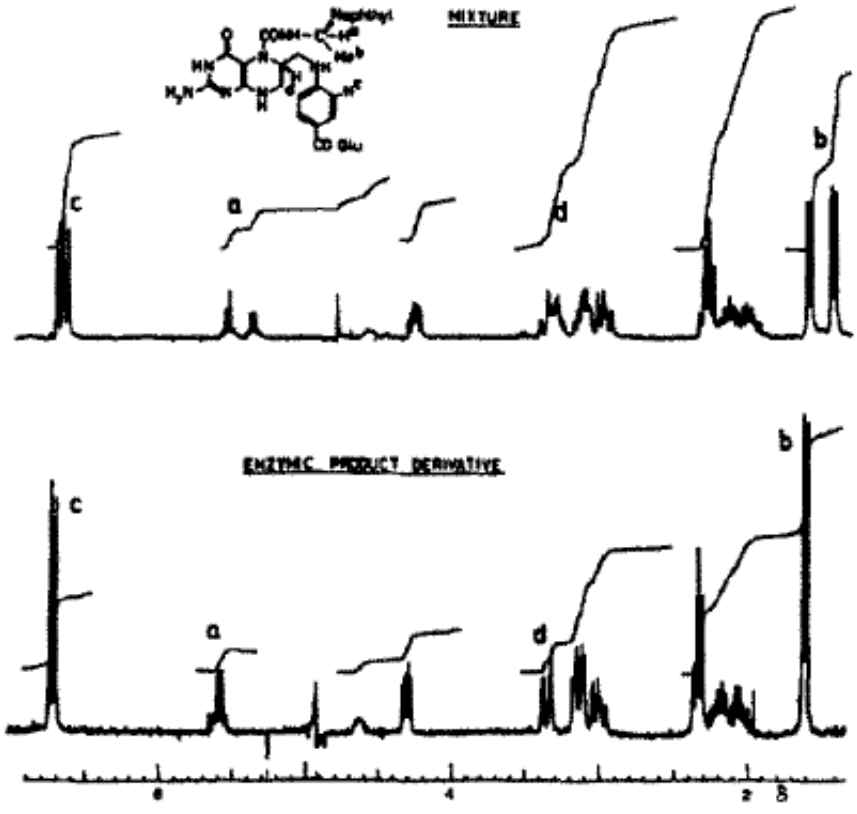


Figure 2 250 MHz nmr of derivatised Tetrahydrofolate diastereoisomers

(*Id.*).

2. "A pharmaceutical composition"

Plaintiffs assert that Rees 1986 did not disclose "a pharmaceutical composition" because "[n]o pharmaceutical composition was prepared" and Defendant's "anticipation 'evidence' consists solely of a tenuous assertion that because Rees 1986 referred to leucovorin as being used as a drug, it somehow therefore disclosed a levoleucovorin pharmaceutical product." (Pls.' Mot. for Summ. J. 17:11–18).

However, Defendant argues that Rees 1986 discloses "a pharmaceutical composition" because, although "the Rees 1986 authors did not actually *make* a pharmaceutical composition," "Rees 1986 disclosed that its techniques made 'the possibility of synthesizing chiral 5-formyltetrahydrofolate (leucovorin) for use in cancer rescue therapy attainable.'" (Def.'s Resp. at 18–19 (quoting Ex. 4 to Decl. of Amanda K. Antons at 2, ECF No. 237–4)).

Additionally, Defendant quotes Federal Circuit case law for the proposition that "anticipation does not require actual performance of suggestions in a disclosure. Rather, anticipation only requires that those suggestions be enabled to one of skill in the art." (*Id.* at 18 (quoting *Novo Nordisk Pharm., Inc. v. Bio-Tech. Gen. Corp.*, 424 F.3d 1347, 1355 (Fed. Cir. 2005)). Defendant additionally contends that Rees 1986 discloses using calcium leucovorin to treat humans for methotrexate rescue, and "[b]ecause Rees 1986 encouraged the creation of a pharmaceutical composition, that pharmaceutical composition was in the public's possession." (*Id.*).

The Court finds that factual issues remain about whether Rees 1986 discloses "a pharmaceutical composition." However, this finding alone does not preclude summary judgment because Plaintiffs also contend that Rees 1986 does not disclose "a mixture of (6S) and (6R) diastereoisomers."

3. "mixture of (6S) and (6R) diastereoisomers"

Plaintiffs contend that Rees 1986 "reported the use of an enzyme, dihydrofolate reductase, with an appropriate recycling system (to make the enzyme function in a catalytic reaction) to make an isomerically pure form of the (6S) isomer of leucovorin" and "produced 910 milligrams (less than 1 gram) of pure (6S) leucovorin." (Pls.' Mot. for Summ. J. 9:21–24). Plaintiffs further contend that Defendant does not have evidence to show that Rees 1986 disclosed the "mixture of (6S) and (6R) diastereoisomers" recited in the '829 Patent claims. (*Id.* 13:13–18). Additionally, Plaintiffs assert that Defendant's expert, Dr. Jones, admitted that Rees 1986 disclosed a single product. As support, Plaintiffs provide an excerpt from the deposition of Dr. Jones:

> Q. Can you read that sentence aloud?
> A. "Reverse phase HPLC cleanly separated the diastereoisomer as formed in non-enzymic reduction; whereas, the product of reduction catalyzed by dihydrofolate reductase was a single peak (Figure 1b)."

> Q. So the authors of Rees '86 actually indicated that it's a single product; right?
> A. Yes, they have.
> Q. Okay. And one of ordinary skill in the art reading that sentence would understand the reference to a single peak to mean a single product; right?
> A. Yes.
> …
> Q. Now, the -- in the next sentence, can you read that one aloud?
> A. "Confirmation of the analysis was obtained using NMR at 250 megahertz (Figure 2); the striking differences are to be seen in protons near to the napthyl group a, b, c, d."
> Q. And the confirmation that's referred to in that sentence is the confirmation that it was a single peak; right?
> A. Not that it was a single peak but that it was a single product, yeah.

(*Id.* 12:20–13:11 (quoting Ex. 2 to Decl. of Amanda K. Antons at 5–6, ECF No. 237–2)).

Moreover, Plaintiffs assert that, although Defendant "contends the shoulder in Figure 1b is clear-and-convincing evidence that the product of Rees 1986 was 'a mixture' of (6S) and (6R) leucovorin diastereoisomers," it "has no evidence to support this contention." (*Id.* 13:13–18). To support this assertion, Plaintiffs provide an excerpt from the deposition of Defendant's invalidity expert, Dr. Martin:

> Q. The HPLC in Rees '86, that's figure 1B –
> A. Okay.
> Q. -- you argue that the shoulder next to the enzymatic peak is a derivatized form of 6R; right?
> A. **I think I said it could be**. I think I said that the retention time of that peak is consistent with its being the R, but on the basis of an LC trace, just on that basis, **it's not possible to conclude** -- well, on that -- the basis of that alone, it's not possible to identify what that is other than to say it has a retention time consistent with its being 6R.
> Q. Right. So it -- the retention time is consistent with the 6R peak, but you can't exclude the possibility that it's something else, can you?
> A. No.
> …

> Q. You're saying that the two pieces of evidence, figure -- figure 1B and figure 2 in Rees '86, suggest that the shoulder may be the 6R isomer; right?
> A. **It -- it may be, could be.**
> Q. But not conclusively that it is.
> A. No, I can't be -- I mean the -- the -- there's really not -- the -- the peaks are not large enough in the NMR spectrum for one to be totally certain. It just -- everything -- these two pieces of information are consistent with that being R.

(*Id.* 13:18–14:7 (quoting Ex. 3 to Decl. of Amanda K. Antons at 14–16, ECF No. 237–3). Finally, Plaintiffs assert that the applicants of the '829 Patent overcame rejections based on Rees 1986 "by showing that Rees 1986 made pure (6S) leucovorin: no (6R) leucovorin was present." (*Id.* 14:11–15).

On the other hand, Defendant asserts that it "has offered clear and convincing evidence from expert analyses of the prior art data and the principles of chemistry that Rees 1986 produced some (6R) diastereoisomer." (Def.'s Resp. at 17). As support, Defendant cites the Opening Expert Report of Dr. Martin, asserting that Figure 1b of Rees 1986 (the HPLC chromatogram) "shows a shoulder immediately to the right of the main peak" and "[t]he shoulder … elutes at the same location as the (6R) diastereoisomer in the chromatogram of the (6R,S) mixture, and it conforms to the retention time that one would expect for (6R) diastereoisomer." (Ex. 1 to Decl. of Stephen F. Martin ¶ 144, ECF No. 246–1). Additionally, Dr. Martin opines that Figure 2 of Rees 1986 (the NMR spectra):

> reveals the presence of very small peaks, which do not have the random appearance of noise, at a chemical shift to the right of the "b" protons. Based upon the (6R,S) spectrum, this position is exactly where one of ordinary skill in the art would expect a signal from the (6R) diastereoisomer. … The appearance of these small peaks to the right of the "b" peak thus supports identification of the shoulder in the HPLC chromatogram as being the (6R) isomer.

(*Id.* ¶ 145). Moreover, Dr. Martin opined "that Rees 1986 … [does] not disclose entirely pure

(6S) diastereoisomer, but instead disclose[s] a product having approximately 99% purity." (*Id.* ¶ 152). As additional support, Defendant cites to Dr. Jones' deposition testimony, acknowledging "the Rees 1986 authors called their figure a 'single peak,' but '*for them to say that it is a single peak is incorrect because it is not a single peak. It is a peak with a small shoulder on it*." (Def.'s Resp. at 13 (quoting Ex. 8 to Decl. of John Lanham at 6)). Additionally, Dr. Jones testified "[t]his is a blow-up of the enzymic product derivative from figure 2 of the Rees paper … And if one looks underneath the right-hand doublet that has been superimposed from the top spectrum representing (6R), you can see that there is a tiny doublet underneath it corresponding, in my view, to the 2 percent of the (6R) enantiomer of the enzymic product." (*Id.* at 7).

The Court finds that factual issues remain about whether Rees 1986 discloses "a mixture of (6S) and (6R) diastereoisomers. Because there are genuine issues of material fact of what Rees 1986 teaches, the Court denies summary judgment on whether Rees 1986 anticipates the disputed claims. Finally, because the Court finds that genuine issues of material fact exist regarding anticipation in light of Rees 1986, the Court also finds that genuine issues of material fact exist regarding obviousness in light of Rees 1986. *See Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 ("a disclosure that anticipates under § 102 also renders the claim invalid under § 103, for 'anticipation is the epitome of obviousness'").

C. Plaintiffs' Motion for Summary Judgment of No Inequitable Conduct

Plaintiffs assert it is entitled to summary judgment of no inequitable conduct. Inequitable conduct occurs when the patent applicant fails to disclose material information, or submits false material information, with an intent to deceive the United States Patent and Trademark Office ("PTO"). *Kingsdown Med. Consultants, Ltd. v. Hollister Inc.*, 863 F.2d 867, 872 (Fed. Cir. 1988); *see also* 37 C.F.R. § 1.56 ("Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the

[Patent] Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section."). Inequitable conduct is an equitable defense to patent infringement that, if proved, bars enforcement of a patent. *Therasense, Inc. v. Becton, Dickinson & Co.*, 649 F.3d 1276, 1287 (Fed. Cir. 2011) (en banc). "To prove inequitable conduct, the challenger must show by clear and convincing evidence that the patent applicant (1) misrepresented or omitted information material to patentability, and (2) did so with the specific intent to mislead or deceive the PTO." *In re Rosuvastatin Calcium Patent Litig.*, 703 F.3d 511, 519 (Fed. Cir. 2012) (citing *Therasense*, 649 F.3d at 1287). Furthermore, "materiality and intent must be separately established." *Id.*

The facts are relatively undisputed. The original application of the '829 Patent was filed on September 2, 1987 and was issued on December 31, 2002, following a series of continuation applications. (*See* U.S. Patent No. 6,500,829). The '829 Patent issued with fourteen (14) claims. (*Id.*). On both July 25, 1994 and April 18, 1995, the prosecuting attorney, Stephen Bodenheimer, filed a Continuation Application. (Ex. 1 to Decl. of John Lanham at 19–26, ECF No. 247–1). For each Continuation Application, Mr. Bodenheimer counted Claim 40, which eventually became Claim 13 of the '829 Patent, as a dependent claim for fee-calculation purposes. (*See id.* at 20, 24). Additionally, each Continuation Application authorized the PTO to charge additional fees or credit any overpayment. (*Id.*).

Moreover, on March 10, 1997, Mr. Bodenheimer filed an amendment to amend Claim 40, changing the first word from "The" to "A." (*Id.* at 27). Mr. Bodenheimer stated the amendment was to "correct minor informalities," but the amendment was rejected by the PTO as "not necessary." (*Id.* at 28). Furthermore, on August 29, 2012, counsel for Plaintiff Spectrum, Andrew Lawrence, filed a Request for Certificate of Correction with the PTO to change the first word of Claim 13 from "The" to "A." (*See* Ex. 22 to Decl. of John Lanham, ECF No. 247–22). In the Request, Mr. Lawrence stated "[t]he errors now sought to be

corrected are inadvertent typographical errors the correction of which does not involve new matter or require reexamination." (*Id.* at 3). Mr. Lawrence also stated "[t]he amendment confirms that claim 13 should be construed as being directed to an independent invention than that recited in claims 10 and 11." (*Id.*). The Certificate of Correction was granted on October 2, 2012. (*See* U.S. Patent No. 6,500,829).

Defendant asserts that Plaintiffs committed inequitable conduct before the PTO by designating Claim 13 as dependent for fee-calculation purposes and for requesting the Certificate of Correction of Claim 13. (*See* Def.'s Resp. at 24–36).

1. Materiality

The party alleging inequitable conduct may prove the materiality prong in one of two ways. Most commonly, the party attempts to establish "but-for materiality" by providing "proof that the patentee withheld or misrepresented information that, in the absence of the withholding or misrepresentation, would have prevented a patent claim from issuing." *Ohio Willow Wood Co. v. Alps S., LLC*, 735 F.3d 1333, 1345 (Fed. Cir. 2013). Alternatively, a court will presume materiality where the party alleging inequitable conduct proves that "the patentee has engaged in affirmative acts of egregious misconduct, such as the filing of an unmistakably false affidavit." *Therasense*, 649 F.3d at 1292.

i. But-for Materiality

First, Plaintiffs assert that "but-for" materiality cannot be shown in regards to the determination and payment of filing fees during the prosecution of the '829 Patent because "[t]his Court has determined that claim 13 is a dependent claim," and "the appropriate fee with respect to application claim 40 (which became '829 patent claim 13) was for a dependent claim." (Pls.' Mot. for Summ. J. 33:22–24). Additionally, Plaintiffs assert that "***nothing*** was withheld" from the PTO. (Pls.' Reply 17:11). More specifically, Plaintiffs assert that the "PTO had the claims, and the ability—indeed, Mr. Bodenheimer's express permission—to charge him

additional fees for any underpayment." (*Id.* 17:11–12). On the other hand, Defendant asserts that "Mr. Bodenheimer's representations regarding the number of independent claims in the '829 patent were a 'but-for' cause for Claim 13 issuing without an additional fee." (Def.'s Resp. at 33).

The Court finds that "but-for" materiality cannot be shown in regards to the determination and payment of filing fees during the prosecution of the '829 Patent. Plaintiffs correctly acknowledge that "Claim 13 is, and always was, a dependent claim." (Pls.' Reply 16:17). When Mr. Bodenheimer determined and paid the filing fees, representing Claim 13 as a dependent claim, the PTO issued Claim 13 as a dependent claim. Indeed, this Court held in its Claim Construction Order that Claim 13 was a dependent claim. Therefore, Mr. Bodenheimer's determination and payment of filing fees was not a "but-for" cause of the PTO issuing Claim 13 as an independent claim—Claim 13 is, and always was, a dependent claim.

Second, Plaintiffs assert that "but-for" materiality cannot be shown in regards to the Certificate of Correction of Claim 13 of the '829 Patent because "Claim 13 was no more an independent claim before the correction than after as this Court found in its claim construction order." (Pls.' Reply 19:23–24). Accordingly, Plaintiffs conclude "[b]ut-for materiality simply does not fit this scenario." (*Id.* 19:24–25). Conversely, Defendant asserts "Mr. Lawrence's certification that the requested change was suitable for a Certificate of Correction under 35 U.S.C. § 255 was the 'but-for' cause of the Certificate of Correction being issued." (Def.'s Resp. at 36).

The Court finds that "but-for" materiality cannot be shown in regards to the Certificate of Correction of Claim 13 of the '829 Patent. The PTO had all the information it needed, including the prosecution history detailing Mr. Bodenheimer's similar amendment that was rejected, to make an informed determination to either grant or deny the Certificate of Correction; nothing was withheld. Moreover, Mr. Lawrence disclosed his intentions in the

Request by stating "[t]he amendment confirms that claim 13 should be construed as being directed to an independent invention than that recited in claims 10 and 11." (Ex. 22 to Decl. of John Lanham at 3, ECF No. 247–22). Finally, the Certificate of Correction did not change the scope of Claim 13 from dependent to independent. (*See* Ct.'s Claim Construction Order at 37:13–14, ECF No. 199 (holding that Claim 13 is a dependent claim)).

ii. Affirmative Egregious Misconduct

First, Plaintiffs assert that affirmative egregious misconduct cannot be shown in regards to the determination and payment of filing fees during the prosecution of the '829 Patent because "there was no misrepresentation; all the required information was presented to and reviewed by the PTO." (Pls.' Mot. for Summ. J. 34:8–10). Conversely, Defendant asserts that the signed statement submitted by Mr. Bodenheimer regarding filing fees were "forms of false declaration" akin to the "unmistakably false affidavits" mentioned in *Therasense.* (Def.'s Resp. at 31–32). However, Plaintiffs contend that "affidavits and declarations are written sworn statements made under oath," and "[f]ee-calculation worksheets are not 'forms of declarations,' they are PTO forms." (Pls.' Reply 18:1–3).

The Court finds the Federal Circuit's decision in *Network Signatures Inc. v. State Farm Mut. Auto. Ins. Co.* particularly instructive on this issue. 731 F.3d 1239 (Fed. Cir. 2013). In *Network Signatures,* State Farm asserted that the patent at issue was unenforceable on the ground that the patentee engaged in inequitable conduct by falsely misrepresenting to the PTO that the patentee's non-payment of the maintenance fee was unintentional. *Id.* at 1240. Additionally, State Farm asserted that the delay in payment of the maintenance fee was not unintentional because the patentee paid the fee only after learning of commercial interest in the patent at issue. *Id.* at 1241. The Federal Circuit affirmed the district court's holding that the patentee's statements to the PTO regarding the delayed payment of the maintenance fee did not rise to the level of affirmative egregiousness of the cases *Therasense* references. *Id.* at 1242.

Moreover, while holding that the patentee's conduct did not constitute inequitable conduct, the Circuit instructed "[o]n matters unrelated to the substantive criteria of patentability, but within the authority of the Director, 'it is almost surely preferable for a reviewing court not to involve itself in the minutiae of Patent Office proceedings and to second-guess the Patent Office on procedural issues at every turn.'" *Id.* at 1243 (quoting *Laerdal Med. Corp. v. Ambu, Inc.*, 877 F. Supp. 255, 259 (D. Md. 1995)). Finally, the Circuit held "[w]e have recognized an 'unwillingness to extinguish the statutory presumption of validity' where the patentee's conduct 'did not affect the issuance of the patent.'" *Id.* at 1243–44 (quoting *Therasense*, 649 F.3d at 1291).

The Court finds that Mr. Bodenheimer's determination and payment of filing fees do not rise to the level of affirmative egregiousness cited in *Therasense*, including perjury, the manufacture of false evidence, and the suppression of evidence. *See, e.g.*, *Keystone Driller Co. v. Gen. Excavator Co.*, 290 U.S. 240, 243 (1993); *Hazel-Atlas Glass Co. v. Hartford-Empire Co.*, 322 U.S. 238, 240 (1944), overruled on other grounds by *Standard Oil Co. v. United States*, 429 U.S. 17 (1976); *Precision Instrument Mfg. Co. v. Auto. Maint. Mach. Co.*, 324 U.S. 806, 816–20 (1945). The Court is unwilling "to involve itself in the minutiae of Patent Office proceedings and to second-guess the Patent Office on procedural issues at every turn." *Network Signatures*, 731 F.3d at 1243 (internal quotations omitted). Likewise, Mr. Lawrence's representations in the Request for Certificate of Correction do not constitute affirmative egregious misconduct.

Accordingly, Plaintiffs' are entitled to summary judgment of no inequitable conduct because Defendant cannot raise a genuine factual dispute that Plaintiffs misrepresented or omitted information material to patentability. Because a genuine issue of material fact does not exist regarding materiality, the Court need not analyze whether Plaintiffs acted with specific intent to deceive.

IV. CONCLUSION

IT IS HEREBY ORDERED that Defendant's Motion for Summary Judgment of Non-Infringement of Claims 5–9 is **GRANTED**. Defendant does not infringe Claims 5–9 of the '829 Patent either literally or under the doctrine of equivalents.

IT IS FURTHER ORDERED that Plaintiffs' Motion for Summary Judgment is **GRANTED in part and DENIED in part**. Plaintiffs are not entitled to summary judgment of no invalidity in light of Rees 1986. Whether the '829 Patent is invalid as anticipated or obvious in light of Rees 1986 remain as issues for trial. Additionally, Plaintiffs are entitled to summary judgment of no inequitable conduct.

DATED this 29th day of December, 2014.

Gloria M. Navarro, Chief Judge
United States District Judge